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PRINCIPAL INVESTIGATOR(S): Doctor Nancy Krieger

CONTRACTING ORGANIZATION: Kaiser Foundation Research Institute
Oakland, California 94619-3433

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This study addresses two questions: (1) how does prevalence of prognostic biomarkers in old, archival paraffin-embedded tumor biopsy specimens obtained from 50 Asian, 50 black, and 50 white women diagnosed with breast cancer in Oakland, CA between 1966 and 1990 compare across racial/ethnic groups and to that observed among recent paraffin-embedded speciments, and (2) what is the relationship of these biomarkers to survival, controlling for other biological and socioeconomic risk factors that affect survival? In Year 1, we have, as planned: (a) abstracted medical chart data on tumor characteristics and treatment for all 150 women, (b) appended these data to an existing database with the women's sociodemographic and reproductive characteristics, (c) determined their vital status as of December 31, 1994, (d) located tumor blocks for 135 of these women, and (e) measured, by immunohistochemistry/image analsis, the following prognostic biomarkers: estrogen, progesterone, androgen, and epidermal growth factor receptors, cathepsin-D, her-2/neu, ps2, p53, Ki67, and DNA ploidy. Tasks for Year 2 include: (a) appending the assay and vital status data to the study's data base, (b) comparing biomarker distribution among the cases' and more recent biopsy specimens, and (c) describing and comparing biomarker distributions and prognostic values by race/ethnicity and social class.

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Introduction

Survival from breast cancer among women varies by race/ethnicity (1-14) and social class (9-20). As compared to white women, survival rates are lower among black women and American Indian women, higher among Japanese and Chinese women, and comparable among Hispanic women (all groups combined; survival is poorer among Puerto Rican as compared to white women)(1-14). Survival rates are also inversely related to socioeconomic position, such that working class and poor women survive less long than professional and more affluent women (9-20).

To date, reasons for racial/ethnic and socioeconomic inequalities in breast cancer survival remain unclear. Some research suggests that late stage at diagnosis (as related to lack of access to medical care) contributes to these patterns, but other studies indicate that survival differences persist even after taking into account stage at diagnosis (3-5,11,16). Thus, other factors may be at issue, including differences in tumor aggressiveness and responsiveness to treatment, as related to hormone receptor status and other tumor properties (4,6,7,15). Termed "prognostic biomarkers," these tumor properties include such oncogenes as her-2/neu, p53, and h-ras, the cytoplasmic protein ps2 and protease cathepsin-D, markers of cell growth such as the Ki67 growth index and DNA ploidy, and presence or absence of receptors for estrogen, progesterone, and epidermal growth factor (6,7,15,21-37).

Presently, little is known about whether the prevalence--and also predictive value--of prognostic biomarkers for breast cancer varies by race/ethnicity and social class (6,7,15). Most research on these biomarkers has been based on samples of women who are chiefly or exclusively white or whose race/ethnicity has not been specified, and most studies also have not included information regarding the socioeconomic characteristics of their study populations (21-37).

More specifically, only four studies to date have sought to determine if the distribution of breast cancer prognostic biomarkers differs by race/ethnicity or social class (6,7,15,38). Three of these focused on racial/ethnic differences and were conducted in the United States (6,7,38). One case-control study compared the presence of a rare allele of the protooncogene h-ras among white and black women and found that the relationship between risk of breast cancer and presence of this allele was three to six times stronger among the black women and was also associated with younger age at diagnosis, more aggressive tumors, and poorer survival (38). Another study observed that black women were more likely than white women to have p53 gene alterations associated with poorer prognosis (6), while a third study found no racial/ethnic differences among breast tumors from black, white, and Hispanic women for p53, DNA ploidy, HER-2/neu (7); in this latter study, however, black and Hispanic women were less likely than the white women to have tumors positive for estrogen and progesterone receptors. None of these three studies included any information on the socioeconomic characteristics of their study populations. A fourth study, performed in Britain, focused on breast cancer prognostic factors in relation to socioeconomic deprivation among white women, and found no difference between poor and affluent women for tumor size, nodal status, grade, and estrogen receptor status (15).

To gain additional understanding of racial/ethnic and socioeconomic disparities in breast cancer survival, it would thus be useful to compare distributions and prognostic significance of breast cancer prognostic biomarkers in women of diverse racial/ethnic and socioeconomic groups. One efficient way to make these comparisons would be to conduct a retrospective cohort analysis, using archived tumor biopsy specimens of women previously diagnosed with breast cancer. This design would permit comparing distributions of prognostic biomarkers among women at time of diagnosis, stratified by race/ethnicity and social class, and also evaluating predictive values of the biomarkers among women in the different racial/ethnic and socioeconomic strata.

Knowledge about predictive values by length of survival would be especially important, because most studies of breast cancer prognostic biomarkers have had relatively short follow-up periods (typically only one to four years), and evidence suggests that some biomarkers may be more predictive of short-term and others of long-term survival (21-37). The short follow-up period of these studies in part stems from their reliance upon fresh, as opposed to archived, tumor biopsy specimens. Little is known, moreover, about the validity of assays performed on older, archived biopsy specimens, and whether they yield results comparable to those performed on fresh specimens; to our knowledge, no study has directly examined this issue. Thus, although it would be desirable to assess distribution and long-term predictive value of breast cancer prognostic biomarkers using archived biopsy specimens obtained from women with extended follow-up, and stratified by race/ethnicity and social class, it would be necessary first to assess the validity of assays performed upon older specimens.

Accordingly, we designed our project to answer to the following questions:

(1) How does the prevalence of prognostic biomarkers in old, archival paraffin-embedded tumor biopsy specimens obtained from a sample of 50 Asian, 50 black, and 50 white women diagnosed with breast cancer in Oakland, CA between 1966 and 1990 compare across racial/ethnic groups, and to that observed among recent paraffin-embedded specimens?

(2) What is the relationship of these biomarkers to survival, controlling for other biological and socioeconomic risk factors that affect survival?

Prognostic biomarkers, to be measured by immunohistochemistry/image analysis, include: estrogen, progesterone, androgen, and epidermal growth factor receptors, cathepsin-D, her-2/neu, ps2, p53, Ki67, and DNA ploidy. Follow-up to ascertain vital status extends through December 31, 1994, thus allowing a follow-up period of up to 4 to 28 years.

We will use chi-square analyses, as performed by the statistical program PC-SAS (39,40), to conduct univariate and age-adjusted comparisons of the distribution of the biomarkers among the white, black, and Asian women, both stratified by and controlling for socioeconomic position. Logistic regression analyses (39,41), as performed by the statistical program EGRET (42), will be used for multivariate comparisons controlling for additional potential confounders, e.g., stage, grade, histologic type, nodal status, body mass

index, and reproductive history. To compare survival rates among the white, black, and Asian women, we will use two different approaches: Kaplan-Meier survival analyses and Cox proportional hazard regression analyses (39,43), both as performed by the statistical program EGRET (42). These analyses will evaluate the relationship between the presence of the selected biomarkers and length of survival, adjusting for other biological and socioeconomic risk factors.

Body

To conduct our retrospective cohort study, we are analyzing data collected on 50 Asian, 50 black, and 50 white women who were diagnosed with breast cancer between 1966 and 1990 in Oakland, CA. These women were part of a recently completed nested case-control study of the relationship between exposure to organochlorines and risk of breast cancer (44). The cases and controls included in this study were selected from a cohort of women who took the multiphasic examination offered by the Kaiser Permanente Medical Care Program (KPMCP) between 1964 and 1969. Data have already been collected on the subjects' sociodemographic and reproductive characteristics at the time of their multiphasic examination and on the cases' tumor characteristics (stage, grade, laterality) and also age and menopausal status at diagnosis. Pertinent characteristics of these women with breast cancer are provided in the table, below:

Selected sociodemographic, reproductive, and tumor characteristics of 150 women diagnosed with breast cancer, 1966-1990, Oakland, CA

Characteristic	Total (n=150)	White (n=50)	Black (n=50)	Asian (n=50)
Age at multiphasic exam (years: mean, SD)	45.2 (9.6)	49.4 (10.6)	45.2 (8.6)	40.9 (7.4)
Education* (%)				
< High school	11.3	10.0	18.0	6.0
≥ High school, < 4 yrs college	68.0	56.0	68.0	80.0
≥ 4 yrs college	19.3	30.0	14.0	14.0
Unknown	1.3	4.0	0.0	0.0
Social Class composition of block-groupt (%)				
< 66% working class	31.3	38.0	22.0	34.0
≥ 66% working class	66.7	58.0	78.0	64.0
Unknown	2.0	4.0	0.0	2.0
Poverty composition of block-groupt (%)				
< 20% below poverty	78.7	90.0	62.0	84.0
≥ 20% below poverty	19.3	6.0	38.0	14.0
Unknown	2.0	4.0	0.0	2.0
Birthplace (%)				
United States	74.7	72.0	82.0	70.0
Foreign	17.3	24.0	10.0	18.0
Unknown	8.0	4.0	8.0	12.0
Age at breast cancer diagnosis (years: mean, SD)	59.4 (10.5)	61.3 (11.0)	61.2 (9.8)	55.7 (9.7)
Year of diagnosis (%)				
1966-1972	13.3	16.0	6.0	18.0
1973-1977	13.3	22.0	6.0	12.0
1978-1982	23.3	28.0	30.0	12.0
1983-1990	50.0	34.0	58.0	58.0

Selected sociodemographic, reproductive, and tumor characteristics of 150 women diagnosed with breast cancer, 1966-1990, Oakland, CA (cont.)

Characteristic	Total (n=150)	White (n=50)	Black (n=50)	Asian (n=50)
Menopausal status at diagnosis (%)				
Premenopausal	20.0	18.0	14.0	28.0
Menopausal, age at menopause:				
< 45 years	17.3	8.0	40.0	4.0
45-55 years	47.3	58.0	30.0	54.0
≥ 55 years	10.0	10.0	10.0	10.0
Menopausal status unknown	5.3	6.0	6.0	4.0
Tumor stage (%)				
Local	64.7	58.0	64.0	72.0
Regional	30.7	34.0	32.0	26.0
Distant	2.7	6.0	2.0	0.0
Unknown	2.0	2.0	2.0	1.0
Tumor size (mm: mean, SD)	26.6 (18.8)	20.5 (13.8)	30.4 (20.4)	28.1 (19.9)

* Characteristic as of time of multiphasic examination
† Referring to the census-block group, i.e., immediate residential neighborhood, where the case lived at the time of the multiphasic examination

The tasks required to conduct our study, as described in our initial proposal, are:

Task 1, Obtain medical charts and tumor blocks, Months 1-2:

a. Order medical charts; once receive them, abstract information on tumor characteristics and surgical accession number, make copy of pathology report
b. Using surgical accession number, order cases' tumor blocks from Central Repository

Task 2, Prepare blocks for delivery to laboratory, Months 3-4:

a. Once receive boxes of tumor blocks, sort through them to locate the desired blocks (and indicate position in boxes, so they can be returned to their original location)
b. Label blocks for analysis by laboratory; indicate case identification number and attach pathology report to blocks for each case

Task 3, Laboratory analysis for selected biomarkers, Months 5-14:

a. Establish data system for linking assay results to each cases' identification number and for keeping track of which blocks have been analyzed
b. Conduct immunohistochemical/image analysis for estrogen, progesterone, and epidermal growth factor receptors, cathepsin-D, her-2/neu, ps2, p53, h-ras, and ki67 (defined as positive or negative).
c. Enter assay results into ASCII file
d. Compile summary data of prevalence of the same biomarkers for paraffin-embedded specimens for breast cancer cases diagnosed in the early 1990s

Task 4, Mortality search, Months 13-14:

a. Determine vital status of each case, as of 12/31/94, using the MORTLINK file
b. Enter vital status of each case into ASCII file

Task 5, Assemble data base, Month 15:

a. Link assay data and vital status data to existing data file
b. Check new data set to ensure the data are accurate

Task 6, Data analysis, return blocks, Months 16-21:

a. Compare prevalence of biomarkers in the study's archival specimens to those of the recently-diagnosed cases
b. Conduct univariate and multivariate analyses comparing prevalence by race/ethnicity and socioeconomic position
c. Conduct Kaplan-Meier survival analysis and Cox regression analyses to evaluate the association of these biomarkers with survival among women in and across the three racial/ethnic groups, adjusting for other known biologic and socioeconomic risk factors for poor survival
d. Return blocks to Central Repository

Task 7, Prepare manuscript and talks based on study findings, Months 22-24

As of the time of preparing this first annual report (end of month 12), we have, in accordance with our timeline, completed Tasks 1, 2, and 4, and have nearly completed Task 3. We outline our results, to date, for each task below. Tasks 1, 2, and 4 were performed at the Division of Research of the Kaiser Foundation Research Institute (Oakland, CA), and Task 3 was (and is being) performed at Aeron Biotechnology (San Leandro, CA).

Task 1, Obtain medical charts and tumor blocks, Months 1-2:

a. Order medical charts; once receive them, abstract information on tumor characteristics and surgical accession number, make copy of pathology report

We were able to locate medical charts for all 150 study subjects, and make copies of their pathology reports. We abstracted data on the following items for each study subject:

- Medical record number
- Name
- Date of birth
- Social security number
- Date of tumor diagnosis
- Date of tumor biopsy
- Surgical accession number
- Use of any hormonal medication in month prior to biopsy
- Use of any other medication in month prior to biopsy
- Tumor characteristics and treatment data:
  - Lymph node involvement
  - Date of first definitive treatment for tumor, including: surgery, radiation, chemotherapy, hormone therapy, immunotherapy
- Vital status at end of follow-up (6/30/94) and if dead, cause(s) of death, autopsy

A copy of the data abstraction form is attached (see Appendix).

These data were entered into a data file, checked for accuracy, and merged into the pre-existing data set, containing data on

the study subjects' sociodemographic and reproductive profile at the time of their multiphasic examination and on the cases' tumor characteristics (stage, grade, laterality) and also age and menopausal status at diagnosis.

b. Using surgical accession number, order cases' tumor blocks from Central Repository

We were able to identify the surgical accession number for all 150 study subjects and order their tumor blocks.

Task 2, Prepare blocks for delivery to laboratory, Months 3-4:

a. Once receive boxes of tumor blocks, sort through them to locate the desired blocks (and indicate position in boxes, so they can be returned to their original location)

We were able to locate tumor blocks for 135 (90%) of the 150 study subjects. The number of blocks per study subject ranged from 1 to 25. We could not locate tumor blocks for 15 women for the following reasons: (a) in 2 cases, the biopsy was not done at Kaiser, (b) in 11 cases, we could not locate the blocks (they were not in the storage boxes in which they were supposed to be contained), and (c) in 2 cases no biopsy was done.

b. Label blocks for analysis by laboratory; indicate case identification number and attach pathology report to blocks for each case

We labeled all identified blocks with their case identification and attached pathology reports to the blocks for each case. Each group of blocks and the patients' pathology report (name effaced) were placed in separate envelopes, and put into four large cardboard boxes, which were then transported from the Division of Research of the Kaiser Foundation Research Institute to Aeron Biotechnology, where the assays would be performed.

Task 3, Laboratory analysis for selected biomarkers, Months 5-14:

a. Establish data system for linking assay results to each cases' identification number and for keeping track of which blocks have been analyzed

At Aeron Biotechnology, staff opened the envelopes and filed the pathology reports in chronological order, using the case identification number to link records. Tumor blocks have been and are being keep in their marked envelopes, except for when subject to analysis.

A worksheet was created at Aeron Biotechnology for recording assay results (see Appendix). An ASCII file was then created that contains all of the information on the worksheet, plus an identifier to indicate if the tumor marker is: negative (0), positive (1), or not analyzable (2).

b. Conduct immunohistochemical/image analysis for estrogen, progesterone, and epidermal growth factor receptors, cathepsin-D,

her-2/neu, ps2, p53, h-ras, and ki67 (defined as positive or negative).

The pathology reports were reviewed to determine which block(s) should be analyzed for tumor markers. The block of choice was listed on the pathology report and the histotechnician was instructed to cut 12 thin sections from each case. Each slide was labeled with the pathology number, and slides were stored in marked slide boxes until assayed (usually within one week).

One H&E slide was prepared from each group and viewed under the microscope to assure the block contained tumor and that the tumor type and description were consistent with the pathology report. If so, the remaining slides were analyzed for tumor markers.

Slides were analyzed for the following tumor markers: estrogen receptor, progesterone receptor, androgen receptor, epidermal growth factor receptor, Her2/neu, cathepsin-D, p53, ps2, Ki67, and DNA ploidy. Immunohistochemical staining results were read and recorded on the worksheet. Analyses were performed for all 135 study subjects whose blocks were delivered to Aeron Biotechnology.

c. Enter assay results into ASCII file

Staining information from the worksheets has been entered into the ASCII file. The data file is currently being checked for accuracy and will be delivered to the Division of Research in early October 1995.

d. Compile summary data of prevalence of the same biomarkers for paraffin-embedded specimens for breast cancer cases diagnosed in the early 1990s

A summary of the prevalence of the same biomarkers for recent tumors has been compiled and is available for comparison to the study data base. Preliminary inspection of the data indicate that the assay values for the older, archived specimens accord well with those found for recent tumors, similar to what we found in the pilot study (based on archived tumor blocks from 35 cases) that we conducted prior to submitting our grant proposal.

Task 4, Mortality search, Months 13-14:

a. Determine vital status of each case, as of 12/31/94, using the MORTLINK file

MORTLINK, a computerized mortality linkage search program owned and operated by the Division of Research, was used to ascertain the vital status of each case, as of 31 December 1994. This program, updated and modified from the CAMLIS system (45), performs a linkage of personal identifiers and descriptors (e.g. name, social security, gender, birth date, race, etc.) of Kaiser Permanente Medical Care Program (KPMCP) members to computerized

death certificates of the State of California. Potential matches are assigned a weighted score based on probabilistic and deterministic decision criteria.

All known members of KPMCP through 31 December 1994 underwent a mortality search using this system and previously available computerized California Death Certificates for 1966 through 1994. This was accomplished by linking a KPMCP membership file of both current and known (historical) members to the computerized death certificate files. All matches of a known KPMCP member with one or more individuals whose death record is on the tapes are maintained in a computerized file. Multiple matches are generated when the data on more than one death certificate provides a sufficient match to generate a weighted probability.

For this study, we searched the computerized file of potential matches for the names and medical record numbers of the 150 women in this study. All 48 matches generated from this search were of a KPMCP member and single death certificate match. Drs. Van Den Eeden and Krieger manually reviewed the 48 matches to evaluate the quality of the matches. In each instance, the matches were judged to be strong, as reflected in the match weights:

Match Weight	Count	(%)
2.3-5.9	1	(2%)
6.0-9.9	11	(23%)
10.0-19.9	25	(52%)
20.0+	11	(23%)
Total	48	(100%)

All matches but one had a match weight of over 6.9. For comparison purposes, in virtually all large mortality studies undertaken at DOR, a weight of 6 is usually judged to be a legitimate match. The choice of this weight is based on manual review of thousands of potential matches augmented with additional data available at KPMCP. The single study women with a match under 6 (match weight = 2.3) occurred because the birth month and year were each off by one digit (1/06/98 according to KPMCP data, but 12/06/97 according to death certificate data), and the social security number was also mismatched. Past experience has shown that women, especially in this age range, often use another social security number, usually their husbands. Thus, the mismatched social security number was not considered sufficient to judge this a non-match. Moreover, the name was unusual and spelled the same in both data sources, the data on residence matched, and the KPMCP date of last follow-up was shortly prior to date of death. Based on the experience of the investigators in similar prior studies, these latter factors were judged sufficient to determine a match in this one case.

In summary, 48 of the 150 women were determined to be deceased from our mortality search based on linkage between KPMCP data on each woman and data from the California State Death Certificates.

b. Enter vital status of each case into ASCII file

The vital status of each woman has been entered into a database and the database is being checked for accuracy. Once the database is edited, it will be merged with the main study database.

Remainder of Tasks 3-7:

During the month of October 1995, the assay data (Task 3c) and vital status data (Task 4b) will be linked to the existing data file (Task 5a), two months earlier than anticipated. Tasks 5b through 7 will be completed during the remainder of year two of the grant, as scheduled.

Conclusions

The work of the first year of this project consisted of tasks related to obtaining the data required to answer our study questions. We will analyze these data, as planned, during the second year of the project. Thus, we are not yet in a position to offer any results or conclusions pertaining to our study questions.

We can, however, summarize the major implications of the work completed to date. The most important is that our work demonstrates that it is feasible, at least within the Kaiser Permanente Medical Care Program, to obtain a high proportion (90%) of archived tumor blocks. We also have shown that it is feasible to obtain the medical charts and ascertain vital status of the individuals who underwent these biopsies. These are important results, because they indicate that large-scale studies using such tumor blocks are possible with a high retrieval rate for both tumor blocks and other relevant data (from medical charts and death certificates). Such studies would be very valuable for research on the short- and long-term predictive value of prognostic biomarkers for all types of cancer, not only breast cancer, providing that assay results based on older, archived tumor specimens are valid. Additionally, the work performed to date indicates that it is possible to perform immunohistochemical analyses on older, archived tumor specimens. Preliminary inspection of the data, moreover, indicates that the assay results fall well within the range of acceptable values (as they did in our initial pilot study), thus suggesting that analyses based on older, archived tumor specimens are valid. This conclusion, however, is tentative until we perform the actual data analysis, in year 2 of this project.

In conclusion, work on our study is proceeding according to plan. In our first year, we have demonstrated the feasibility of obtaining the required data to answer our study questions. In the second year, we will analyze these data and thus be able to assess the broader implications of our study for future analyses of prognostic biomarkers for breast cancer and possibly other types of cancer as well.

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APPENDIX

(1) Data abstraction form

(2) Aeron biotechnology worksheet for recording assay results

FACE SHEET

CHART ABSTRACTION FORM

BREAST CANCER PROGNOSIS STUDY

MR #: ___ ___ ___ ___ ___ ___ ___

Chart location			Reviewer	
Location	Status	Volume	Date	Initials

Status: Active = 1, Retired = 6

Comments on quality of data:

Note here if the data seemed consistent or inconsistent, valid or invalid, or if lots of data were missing, or any other outstanding problems or good features about the data for this person.

Appendix 1
Data Abstraction Form

NOTE: INFORMATION ON THIS FACE SHEET IS NOT TO BE ENTERED AS DATA

CHART ABSTRACTION FORM

N. Krieger, 9/8/94

Card: 0 1
1 2

1) IDENTIFICATION

MRC2 a) MR #: ___ ___ ___ ___ ___ ___ ___
3 4 5 6 7 8 9

b) Name: Unknown: BLANK

LNAME Last: ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___
10 11 12 13 14 15 16 17 18 19 20 21 22 23 24

FNAME First: ___ ___ ___ ___ ___ ___ ___ ___ ___ ___
25 26 27 28 29 30 31 32 33 34

MNAME Middle Initial: ___
35

c) Date of birth: Unknown: Month = 99
Day = 99
Year = 9999

Month: ___ ___ Day: ___ ___ Year: ___ ___ ___ ___
36 37 38 39 40 41 42 43

BMOC2 BDAYC2 BYRC2

SSN d) Social Security No.: ___ ___ ___ ___ ___ ___ ___ ___ ___ Unknown: 999 99 9999
44 45 46 47 48 49 50 51 52

2) DATE OF TUMOR DIAGNOSIS AND TUMOR BIOPSY INFORMATION

a) Date of tumor diagnosis:

Unknown: Month = 99
Day = 99
Year = 9999

Month: 53 54 Day: 55 56 Year: 57 58 59 60

DXMOC2 DXDYC2 DXYRC2

b) Date of tumor biopsy:

Unknown: Month = 99
Day = 99
Year = 9999

Month: 61 62 Day: 63 64 Year: 65 66 67 68

BIOPMO BIOPDY BIOPYR

c) Surgical accession number:

69 70 71 72 73 - 74 75 76 77 78 79

SURGACC

Card: 0 2
1 2

MR #: ___ ___ ___ ___ ___ ___ ___
3 4 5 6 7 8 9

3) HORMONE OR OTHER MEDICATION USE DATA AT TIME OF BIOPSY (PRECEDING MONTH)

*** REMINDER (to be filled in, but NOT FOR DATA ENTRY): date of tumor biopsy = ___/___/___, so start of prior year = ___/___/___ and of prior month = ___/___/___ ***

a) Use of any hormonal medication in month prior to biopsy (FILL IN AFTER COMPLETE 3A-3C)

___
10

HORMUSE

1 = Yes
2 = No
9 = Unknown

b) HORMONAL DRUG #1

Type of hormonal medication: specific drug code

___ ___ ___ ___
11 12 13 14

HMED1

[SEE HORMONAL DRUG CODE SHEET]
8888 = unknown, but took hormones
9999 = unknown if took any hormones
0000 = did not take any hormones

Date of prescription, in year prior to biopsy date, closest to date of biopsy

___ ___ / ___ ___ / ___ ___ ___ ___
15 16 17 18 19 20 21 22

HMED1MO HMED1DY HMED1YR

Unknown: Month = 99
Day = 99
Year = 999
Didn't take hormones: 00/00/0000

Number of doses prescribed

23 24 25

HMED1ND

Actual number, if known
888 = unknown number, but prescribed hormone
999 = unknown if took any hormones
000 = did not take any hormones

Number of doses supposed to take per day

26 27

HMED1DD

Actual number, if known
88 = unknown number, but prescribed hormone
99 = unknown if took any hormones
00 = did not take any hormones

Type of hormonal medication: hormone type
[THIS IS TO BE FILLED IN AFTER CHART ABSTRACTION IS COMPLETE]

28 29

HMED1T

01 = Birth control, estrogen-only
02 = Birth control, combined (estrogen + progestin)
03 = Birth control, progestin-only
04 = Hormone replacement therapy, estrogen-only
05 = Hormone replacement therapy, combined (estrogen + progestin)
06 = Hormone replacement therapy, progestin-only
07 = Other hormone, estrogen-only
08 = Other hormone, combined (estrogen + progestin)
09 = Other hormone, progestin-only
88 = Hormone, type unknown
99 = Unknown if took any hormones
00 = did not take any hormones

c) HORMONAL DRUG #2

Type of hormonal medication: specific drug code

30 31 32 33

HMED2

[SEE HORMONAL DRUG CODE SHEET]
8888 = unknown, but took hormones
9999 = unknown if took any hormones
0000 = did not take any hormones

3c (cont.)

Date of prescription, in year prior to biopsy date, closest to date of biopsy

Unknown: Month = 99
Day = 99
Year = 999
Didn't take hormones: 00/00/0000

34 35 / 36 37 / 38 39 40 41
HMED2MO HMED2DY HMED2YR

Number of doses prescribed

Actual number, if known
888 = unknown number, but prescribed hormone
999 = unknown if took any hormones
000 = did not take any hormones

42 43 44
HMED2ND

Number of doses supposed to take per day

Actual number, if known
88 = unknown number, but prescribed hormone
99 = unknown if took any hormones
00 = did not take any hormones

45 46
HMED2DD

Type of hormonal medication: hormone type
[THIS IS TO BE FILLED IN AFTER CHART ABSTRACTION IS COMPLETE]

47 48
HMED2T

01 = Birth control, estrogen-only
02 = Birth control, combined (estrogen + progestin)
03 = Birth control, progestin-only
04 = Hormone replacement therapy, estrogen-only
05 = Hormone replacement therapy, combined (estrogen + progestin)
06 = Hormone replacement therapy, progestin-only
07 = Other hormone, estrogen-only
08 = Other hormone, combined (estrogen + progestin)
09 = Other hormone, progestin-only
88 = Hormone, type unknown
99 = Unknown if took any hormones
00 = did not take any hormones

d) Use of any other type of medication in month prior to biopsy

49
OTHMED

1 = Yes
2 = No
9 = Unknown

e) If so, what type of medication (WRITE IN ANSWER, FOR UP TO SIX DRUGS; NO CODES. IF SOMEONE HAS BEEN PRESCRIBED A DRUG, BUT SOME OF THE REQUESTED INFORMATION IS UNKNOWN, WRITE IN WHAT YOU CAN AND WRITE "UNKNOWN" FOR WHAT CAN'T BE KNOWN BECAUSE THE INFORMATION IS NOT IN THE CHART)

Drug	Name	Date Prescribed (closest to biopsy date) (MM/DD/YYYY)	No. of doses	No. of doses/day	Reason for prescription
1		__/__/____			
2		__/__/____			
3		__/__/____			
4		__/__/____			
5		__/__/____			
6		__/__/____			

f) Drug Codes (to be assigned later, if relevant)

Drug	Code
1	50 51 52 53
2	54 55 56 57
3	58 59 60 61
4	62 63 64 65
5	66 67 68 69
6	70 71 72 73

Card: 0 3
1 2

MR #: ___ ___ ___ ___ ___ ___ ___
3 4 5 6 7 8 9

4) TUMOR CHARACTERISTICS AND TREATMENT DATA

a) Lymph node involvement

___ ___
10 11

LYMPH NOD

00 - all nodes examined negative
1-96 - number positive
97 - positive, but number unknown
98 - no nodes examined (none removed)
99 - unknown

**** NOTE ON CODING ITEMS 4B-4G *****

1) If underwent specified treatment, and exact start date is known, fill in actual values

2) If underwent specified treatment, but exact start date is unknown, fill in each part of the date that is known with the actual value, and fill in the unknown portion of the date as follows:

Month - 88
Day - 88
Year - 8888

3) If unknown if underwent specified treatment, fill in as follows:

Month - 99
Day - 99
Year - 9999

4) If did <u>not</u> undergo specified treatment, fill in as follows:

Month - 00
Day - 00
Year - 0000

b) Date first course of definitive treatment started for this tumor (BASED ON ITEMS 4C-4G)

Month: 12 13 TREATMO Day: 14 15 TREATDY Year: 16 17 18 19 TREATYR

c) Date definitive surgery first performed

Month: 20 21 SURGMO Day: 22 23 SURGDY Year: 24 25 26 27 SURGYR

d) Date radiation therapy started

Month: 28 29 RADIATMO Day: 30 31 RADIATDY Year: 32 33 34 35 RADIATYR

e) Date chemotherapy started

Month: 36 37 CHEMOMO Day: 38 39 CHEMODY Year: 40 41 42 43 CHEMOYR

f) Date hormone therapy started

Month: 44 45 HORMTMO Day: 46 47 HORMTDY Year: 48 49 50 51 HORMTYR

g) Date immunotherapy started

Month: 52 53 IMMUNOMO Day: 54 55 IMMUNODY Year: 56 57 58 59 IMMUNOYR

Card: 0 4
1 2

MR #: ___ ___ ___ ___ ___ ___ ___
3 4 5 6 7 8 9

5) VITAL STATUS (AS OF END OF FOLLOW UP [FU], DEFINED AS 6/30/94)

a) Last date entered in medical chart (up to 6/30/94)

Unknown: Month = 99
Day = 99
Year = 9999

Month: ___ ___ (10 11) LASTMO
Day: ___ ___ (12 13) LASTDY
Year: ___ ___ ___ ___ (14 15 16 17) LASTYR

b) Vital status as of this date (alive or dead)

___ (18) VSTATUS

1 = Alive
2 = Dead
9 = Unknown

c) Date of death

Month: ___ ___ (19 20) DEATHMO
Day: ___ ___ (21 22) DEATHDY
Year: ___ ___ ___ ___ (23 24 25 26) DEATHYR

Dead, date known: fill in actual date
Dead, but date unknown: fill in unknown values as
MM = 88, DD = 88, YYYY = 8888
Unknown if dead (at end of follow-up):
MM = 99, DD = 99, YYYY = 9999
Alive (at end of follow-up):
MM = 00, DD = 00, YYYY = 0000

e) Immediate cause of death

27 28 29 . 30 31

DTHCAUSE

Known cause of death - ICD-9 code
Dead, cause of death unknown - 8888
Unknown if dead (at end of fu) - 9999
Alive (at end of fu) - 0000

f) Due to or consequence of (#1)

32 33 34 . 35 36

DTHDUE1

Known cause of death - ICD-9 code
Dead, cause of death unknown - 8888
Unknown if dead (at end of fu) - 9999
Alive (at end of fu) - 0000

g) Due to or consequence of (#2)

37 38 39 . 40 41

DTHDUE2

Known cause of death - ICD-9 code
Dead, cause of death unknown - 8888
Unknown if dead (at end of fu) - 9999
Alive (at end of fu) - 0000

h) Autopsy

42

AUTOPSY

Yes - 1
No - 2
Unknown - 9

NANCY, 4/6/95

BREAST CA UPDATED LIST - BY - DR. NANCY KRIEGER

SP SEE TWO (2) ADDITIONS ON PAGE 2 ASSIGNED DRUG CODES

BEVERLY

NUMBER OF PATIENTS	MEDICATION	INDICATION (IF KNOWN)	DRUG CODE
9	PREMARIN .625	04	7901
4	PREMARIN 1.25	04	7902
2	PREMARIN NOS	04	7910
1	CONJ. ESTROGEN .625	04	0082
1	E. ESTROGEN NOS	07	2004
1	ETHINYL ESTRADIOL .02	04	3100
1	ESTROGEN CREAM (VAG)	07	2006
1	PROVERA NOS	06	8403
1	MEDROXYPROGESTERONE (PROVERA)	06	8403
1	OVRAL 21 DAY	02	7300
1	OVULEN NOS	02	7503
	OTHER MEDICATION		
24	HCTZ	HYPERTENSION	100
3	ALDACTONE	HYPERTENSION	101
5	INDERAL	HYPERTENSION	102
2	MAXZIDE	HYPERTENSION	103
1	CALAN SR	HYPERTENSION	104
1	ISMELIN	HYPERTENSION	105
9	DYAZIDE	HYPERTENSION	106
1	MINIPRESS	HYPERTENSION	107
1	HYDRALAZINE	HYPERTENSION	108
2	PROPANOLOL	HYPERTENSION	109
4	RESERPINE	HYPERTENSION	110
3	ALDOMET	HYPERTENSION	111

SPECIFIC MEDICATIONS & ASSIGNED DRUG CODES

NUMBER OF PATIENTS	MEDICATION	INDICATION (IF KNOWN)	DRUG CODE
3	LASIX	HYPERTENSION	112
1	METOROLOL	HYPERTENSION	113
1	CLONIDINE	HYPERTENSION	114
1	ALDACTAZIDE	HYPERTENSION	115
1	DIURIL	HYPERTENSION	116
1	"DIURETIC"	HYPERTENSION	117
1	HYDRO DIURIL	HYPERTENSION	118
1	ESIDRIX	HYPERTENSION	119
1	KAON	POTASSIUM REPLACEMENT	200
1	SLOW K	POTASSIUM REPLACEMENT	201
8	KCL	POTASSIUM REPLACEMENT	202
2	POTASSIUM	POTASSIUM REPLACEMENT	203
1	PROCAN SR	HEART	300
1	NITROGLYCERIN	ANGINA	301
1	PROLOID	THYROID	400
6	L-THYROXINE	THYROID	401
7	THYROID	THYROID	402
1	LITHIUM	BIPOLAR DISORDER	500
5	VALIUM		501
2	LIBRIUM	NERVES	502
1	STELAZINE	EMOTIONAL DIFFICULTIES	503
1	ELAVIL	EMOTIONAL DIFFICULTIES	504
1	ARTANE	EMOTIONAL DIFFICULTIES	505
1	REG U100	DIABETES	600
1	LENTE	DIABETES	601
1	MICRONASE	DIABETES	602
2	NPH	DIABETES	603

SPECIFIC MEDICATIONS & ASSIGNED DRUG CODES

NUMBER OF PATIENTS	MEDICATION	INDICATION (IF KNOWN)	DRUG CODE
2	DIABINESE	DIABETES	604
2	THEODUR	ASTHMA	700
1	ALUPENT	ASTHMA	701
1	INH	ASTHMA	702
1	ALLERGY SHOTS	ALLERGIES	800
1	ANTI HISTAMINE	HAY FEVER	801
2	CHLORTRIMETON	ALLERGIES	802
1	BELLERGAL CREAM	ITCHING	900
1	BENADRYL	SLEEP	1000
1	AMITRIPYLINE	SLEEP	1001
1	DIAMOX	GLAUCOMA	1100
1	BEOPTIC	GLAUCOMA	1101
1	ESKATROL	WEIGHT	1200
1	COMBID	GI DISTRESS	1300
1	LOMOTIL	DIARRHEA	1301
1	BISACODYL	CONSTIPATION	1302
1	CALCIUM	CALCIUM REPLACEMENT	1400
1	TUMS	CALCIUM REPLACEMENT	1401
1	BABY ASPIRIN	TIA's	1500
3	ASA		1501
2	INDOCIN	GOUT/ARTHRITIS	1600
2	EASPIRIN	ARTHRITIS	1601
1	EMPIRIN COMPOUND 65 (CONTAINS CODEINE)	ARTHRITIS	1602
2	MOTRIN	ARTHRITIS	1603
1	DARVON COMPOUND 65	PAIN	1700

BREAST CANCER PROGNOSIS STUDY - DR. NANCY KRIEGER

SPECIFIC MEDICATIONS & ASSIGNED DRUG CODES

NUMBER OF PATIENTS	MEDICATION	INDICATION (IF KNOWN)	DRUG CODE
1	FIORINAL	PAIN	1701
1	BUFFERIN	PAIN	1702
1	TYLENOL ē CODEINE	PAIN	1703
1	MORPHINE SULFATE	PAIN OF LUNG CA	1800
1	CHEMO	LUNG CA	1900
1	TRIPLE SULFA	UTI	2000
4	VITAMINS		2100
1	COD LIVER OIL CAPSULE		2200
1	CHINESE HERBS	(033 23 40)	2300
1	SMALL POX VAC	GOING TO EUROPE	2400

Appendix 2
Worksheet for Recording Study Results

1. ACCESSION #_____ 2. CRD #_____ 3. MR #_____

4. TUMOR TYPE_____

5. GENERAL COMMENT

6. ER TUMOR: _____ % _____intensity

7. COMMENT

8. ER NORMAL: _____ % _____intensity

9. COMMENT

10. PR TUMOR: _____ % _____intensity

11. COMMENT

12. PR NORMAL: _____ % _____intensity

13. COMMENT

14. AR TUMOR: _____ % _____intensity

15. COMMENT

16. AR NORMAL: _____ % _____intensity

17. COMMENT

18. EGFR: _____ % _____intensity

19. COMMENT

20. HER2NEU: _____ % _____intensity

21. COMMENT

22. p53: _____ % _____intensity

23. COMMENT

DNA: PLOIDY %S PHASE

24. FLOW:

25. IMAGE:

26. Ki67: _____ %

27. CATHEPSIN D: _____ % _____intensity

28. pS2: _____ % _____intensity